

**MICHIGAN ENVIRONMENTAL SCIENCE BOARD**

**COUNCIL OF GREAT LAKES GOVERNORS SPECIAL FISH ADVISORY PANEL  
MEETING SUMMARY  
WEDNESDAY, NOVEMBER 30, 1994  
HOLIDAY INN WEST  
LANSING, MICHIGAN**

**PANEL MEMBERS PRESENT**

Dr. Lawrence Fischer, Chair  
Dr. Gary Carlson  
Dr. Joseph Jacobson  
Dr. Barbara Knuth  
Dr. Peter Thomas  
Dr. Kendall Wallace  
Mr. Keith Harrison, MESB Executive Director

**PANEL MEMBERS ABSENT**

Dr. Michael Bolger  
Dr. Martha Radike  
Dr. Mark Roberts

**DMB/EAD SUPPORT STAFF PRESENT**

Mr. Jesse Harrold, Environmental Officer  
Ms. Patricia Hiner, Secretary  
Mr. Alex Morese, Graduate Student Intern

**I CALL TO ORDER**

Dr. Lawrence Fischer, Chair, called the meeting of the Special Fish Advisory Panel to order at 9:30 a.m. Dr. Fischer briefly recapped the last meeting for the benefit of the public attending.

**II EXECUTIVE DIRECTOR REPORT**

Mr. Harrison indicated that he had no report.

**III PRESENTATIONS**

**Dr. Henry Anderson**, Wisconsin Division of Health and Co-chair of the Great Lakes Fish Advisory Task Force (Task Force), presented an overview of the development of the health protection value (HPV) used in the September, 1993 *Protocol for a Uniform Great Lakes Sports Fish Consumption Advisory* (Protocol). A summary of his presentation is contained in Attachment 1.

Dr. Fischer asked why the Task Force did not want to use the standard cancer risk assessment for polychlorinated biphenyls (PCBs) as had the National Wildlife

Federation. Dr. Anderson indicated that the Task Force's concern was not so much that the number obtained from such an analysis was unacceptable or that it could be considered catastrophic if it turned out to be the true estimate. The concern of the Task Force was more about the type of information that has been put out on risk assessment and the ranges of risk that are entailed. The goal of the fish advisory is to inform people and to elicit behavioral change. The Task Force found in talking with anglers that they tended not to believe the assessment.

Dr. Fisher asked if Dr. Anderson felt that numbers arrived at by the U.S. Environmental Protection Agency (USEPA), World Health Organization, and the Agency for Toxic Substances and Disease Registry were derived with the idea of estimating what the actual human No-Observed-Adverse-Effect-Levels (NOAELS) were more for regulatory purposes. Dr. Anderson indicated they were designed to say if one's exposure was below a certain level, then there would not be an effect. It would be a protective number in the sense of guaranteeing that cancer or developmental problems would not occur.

Dr. Fischer asked if the Protocol would be binding on the states once it was finalized. Dr. Anderson stated that the Protocol is really a consensus advisory which no state is required to follow since each state has jurisdiction over its own water bodies or portions of the same water bodies. However, given the multi-state representation and input on the Task Force, it is unlikely that one or more of the states would stray too far from the Protocol.

Dr. Carlson asked whether or not the maximum six recommended annual fish meals were eaten throughout the year or on six consecutive days. Dr. Anderson answered that there were no clear data available on that issue. When looking at lifetime risk, it may not matter.

Dr. Knuth noted that the Protocol states that the advisory is designed to protect children and asked how an adult should interpret it. Dr. Anderson indicated that the Protocol is designed to gain compliance by focusing on peoples' concerns and that child health is something that will motivate behavioral change. Dr. Knuth asked whether the Task Force thought the Protocol provided an appropriate level of protection for other groups. Dr. Anderson answered that the Task Force was comfortable that everyone was covered.

Dr. Wallace asked how it would be determined if the Protocol needed to be driven by a different chemical. Dr. Anderson said that it would be based on the available monitoring data for the lakes. Dr. Wallace also asked how often the Task Force planned to review the fish class and size monitoring data. Dr. Anderson indicated that the review would be based on a three year rolling average to avoid artificial short-term swings. Drs. Wallace and Carlson expressed concern about the manner in which the Task Force used the weight of evidence approach because it was very hard to document and hard for the Panel to review, since the numbers were subjectively agreed on by a number of people.

Dr. Fischer asked if it was fair to summarize that the Task Force's selection of the Protocol's HPV involved an evaluation using a weight of evidence approach of the various data on cancer, reproductive effects and immunological effects, and then selected a value which would be representative of the central tendency of the data reviewed and which would be protective in terms of public health for the most sensitive portion of the population. Dr. Anderson indicated that the Task Force did not set out to look for a value which would necessarily absolutely protect the most sensitive population. The number chosen will protect against a variety of toxic impacts. It is not going to be protective against every possible reference dose (RfD). Dr. Fischer followed by asking if the Task Force did not have any particular health, cancer or developmental outcome in mind when it selected the number, was it selected based on what the Task Force could reach a consensus. Dr. Anderson stated that the process used to develop the HPV was quite involved and that the Task Force relied upon the judgements of its various experts to determine the adequacy of the value to be protective for their area of expertise. It was coincidental that the final number selected was as close as it is to the other, later derived numbers.

Dr. Jacobson asked if the Task Force looked at RfDs based on immune toxicity. Dr. Anderson indicated that it had and found the numbers to be comparable to the HPV.

**Dr. Vernon Miller**, Michigan State University, spoke on preliminary results of a study examining the relationship between awareness of the fish advisory and corresponding behaviors. A summary of his presentation is contained in Attachment 2.

Dr. Carlson asked if there was anyone who derived their high risk beliefs from their own experience, and what type of experience lead them to this belief. Dr. Miller responded that most responses were vague, often a respondent commented on seeing a deformed or sick fish. Dr. Knuth added that based on the studies, the water was also an influential factor. If the water appeared discolored, cloudy, or had an unusual odor, people would relate this to an unhealthy fish.

Dr. Fisher asked if a distinction was made between cancer, heart disease and reproductive risks when questioning respondents on health risks. Dr. Miller stated that most information was gathered from open-ended statements. Specific concern for types of health risks, usually only surfaced if there was a personal connection or experience to a particular illness or disease.

Dr. Anderson asked if the study targeted individuals that fished in areas other than the Great Lakes. Dr. Miller indicated that it did. The survey respondents identified 130 different fishing areas. Twenty-one percent of these areas were identifiable to the Great Lakes.

Dr. Fisher commented that the summary of the research implied a change in beliefs, without a corresponding change in behavior. Dr. Miller replied that the behavior is in consuming fish for food and pleasure and that the method of cleaning the fish merely supports that behavior and is a minor part of the ritual. A person's beliefs prior to

encountering the fish advisory affect whether or not they will even read the advisory or not. Dr. Miller indicated that 33% of the anglers interviewed admitted that they had not read the advisory. Regardless of the advisory, people will still go fishing.

Dr. Knuth commented that if an angler was already trimming his fish prior to reading the advisory, he would respond to the surveyor that he had not changed his fish cleaning method as a result of reading the fish advisory. Another point the Cornell Department of Natural Resources found in its survey was that 39% of the anglers had exceeded the contaminated fish intake advisory level even though they thought they had not. In marketing an advisory, the use of different types of communication strategies is advisable. A more effective advisory would result if an early decision was reached on the Great Lakes standards and testing methods.

Dr. Miller commented that he would prefer to see the fish consumption advisory placed on the front rather than the back page of the fishing regulation and that the state health department be credited with its issuance.

**Dr. John Cicmanec**, USEPA, presented an overview of the current research on PCBs. A summary of his presentation is contained in Attachments 3 and 4.

A unidentified person asked Dr. Cicmanec if there was any significance to the absence of birth weight data for Aroclor 1254. Dr. Cicmanec indicated that Dr. Arnold's paper, which did not refer to Aroclor 1254, was the only reference available at the time the RfD was established. The data acquired from monkey studies at a later date support the original RfD. The birth weights of the treated animals in the later studies were less than and significantly different (.05) than in the control group. This lesser weight remained for at least two months after birth.

Dr. Fischer asked if in the monkey studies, the PCB blood levels were observed. Dr. Cicmanec replied that blood levels were observed and they correlated with the diet intake level.

Dr. Fischer asked if all the Rhesus monkeys used in the Arnold study were obtained from the same or different sources. Dr. Cicmanec replied the monkeys were obtained from two sources where the animals may have been exposed to exotic chemicals. Very little information accompanied these animals about their origin or their previous home. It was presumed at the time that the animals were wild caught. Ninety animals were involved. The animals were held for a time in quarantine and observed for good health and normal body function before conducting the study.

Dr. Fischer asked what the RfD value for Aroclor 1254 was and if the USEPA has ever tried to back calculate to a no-effect level for humans. Dr. Cicmanec indicated that the RfD for Aroclor 1254 is  $2.0 \times 10^{-5}$  mg/kg/day. The USEPA has not calculated a no-effect level for humans. Dr. Jacobson added that Tilson back calculated a daily no-effect dose using Michigan and rodent data.

#### IV PUBLIC COMMENT AND QUESTIONS

Dr. Larry Holcomb, Holcomb Environmental Service, commented that the Panel should be open to new approaches and not take verbatim the interpretations of the USEPA. One consideration would be the use of benchmark doses where possible, such as in the cases of human data where there is a continual range of exposures. A benchmark approach would also take into account data from all the studies rather than relying on a single study. Dr. Holcomb also indicated that he felt the  $5.0 \times 10^{-5}$  mg/kg/day RfD value for Aroclor 1016 and  $2.0 \times 10^{-5}$  mg/kg/day RfD value for Aroclor 1254 were unrealistic and that building uncertainty on uncertainty constituted faulty thinking on the part of the USEPA. Dr. Cicmanec responded that the USEPA was sympathetic to Dr. Holcomb's position but needs to be cognizant of the chemically hyper-sensitive part of the human population. Dr. Holcomb responded that the USEPA should probably develop two RfDs then, one for the hyper-sensitive population and a higher one for the population as a whole. Dr. Cicmanec agreed.

Dr. Clark indicated that the USEPA strongly supports the proposed Protocol, because of the need to reduce human exposure to PCBs, especially for consumers of Lake Michigan fish, and the need to align the current advisory structure, which is based on Food and Drug Administration (FDA) levels, more closely with other values used to protect human health and the environment. The current advisory gives exposures 30-fold higher than the health protection value for frequent fish eaters. It is 75-fold higher than USEPA's value of the reference dose for 1254. Dietary studies by the FDA show that fish in the market place average 20-fold less PCB contamination than those in Great Lakes fish.

The process of bringing together a variety of scientists and regulatory officials to implement public health policy is very difficult. Thirty agencies have been working on it for a decade. The Task Force looked at all the available scientific information and end points - the reproductive outcomes, the teratogenic outcomes, the immune outcomes, the endocrine effect outcomes, the systemic effect, and cancer potential. A purely scientific way would be to devise a fish advisory on each of those end points with an associated range of uncertainty, and target it to each of the consumer groups, but it would be the most complicated fish advisory that ever existed. However, the Task Force had to view all the information and come up with a consensus value that would cover all the end points and the multiple consumer groups. As a consequence, the Task Force did not employ pure science in its approach to the problem. Rather, it employed the best public health approach given the multiple groups looking at a very complicated situation.

The USEPA encourages people to look at the health protection value relative to other results with other derivations. The life-cycle safe concentration, as calculated by the Michigan Department of Natural Resources using Allen's work, is  $2.7 \times 10^{-5}$  mg/kg/day. The USEPA RfD value is  $2.0 \times 10^{-5}$  mg/kg/day. The World Health Organization's value is  $1.0 \times 10^{-4}$  mg/kg/day. The health protection value based on consideration of all these studies, with some emphasis on the Jacobson and Fine work, is  $5.0 \times 10^{-5}$  mg/kg/day.

These are all within a factor of two, which is astonishing considering that they came from different investigations looking at different data bases. As a consequence, the USEPA feels comfortable with the number that has been developed in the Protocol from a public health stand point.

The USEPA is now seeing effects from PCBs, coplanar PCBs, and dioxins at very low levels; for example for dioxins, 1  $\mu$ g/kg of body weight per day for effects on the immune system. Effects on the endocrine system are difficult to quantify in anything other than large studies. From a public health perspective and a regulatory perspective, the uncertainty factors have to be used to try to protect public health until better science becomes available. It took the Task Force a long period of time. Dr. Clark asked the Panel to focus on that effort and the end result rather than looking for absolute scientific purity, which is not possible to obtain in this complex situation.

Dr. Wallace commented that an advisory could be based on objective, sound science and be very complex, and still be worded in such a way to be understandable to the public. Dr. Clark agreed, but said he wants the Panel to understand the underlying complexity of the document. In spite of the fact that all would like to see expansions of studies on neurological and reproductive evaluations, the amount of information that the Task Force looked at was substantial.

Tim Eder, National Wildlife Federation, commented that he appreciated Dr. Anderson's presentation, describing the shortcomings with the current approach, the use of FDA action levels to derive fish consumption advisories, which do not protect public health, and also Dr. Clark's statement that the use of the FDA advice is giving fish eaters greatly increased loads and burdens of exposure. The current approach does not protect health. In some cases, the advice is not only inadequate, but nonexistent. Women of child-bearing age, in particular, are getting no advice regarding consumption of PCB-contaminated fish in the Great Lakes region right now. So despite the shortcomings of the new Protocol, it provides much greater health protection. Although the process was not a rigorously scientific, highly justified process, it was based on very sound science. There has been a lot of criticism of the process, but not a lot of criticism with the end result. But the end result in the new Protocol is better than the one that is currently in existence. It is important to get it out. It is far more important that the communication package is effective in conveying information to the public. The National Wildlife Federation would like to see the communication package go forward before the next fishing season begins.

Dr. Knuth asked Dr. Clark about the USEPA's interpretation of the degree of protectiveness for women of child-bearing age and children vs. other groups, since in the past advisories have treated women of child-bearing age as a separate group. Dr. Clark indicated that studies in the past few years have shown liver toxicity and immune function effects at about the same level as reproductive effects. In terms of the level of protection for women and children, there may be some uncertainty relative to the fact that chemicals in fish do not appear to be the same in laboratory testing. There may be a higher percentage of the higher chlorinated chemicals. The USEPA does not know

how to treat that quantitatively at this point in time. The bottom line is that under the current advisory women and children are above the acceptable risk level.

Ward Hodge, Marlette, Michigan, commented on a newspaper article of March, 1994 in which it was reported that levels of contamination in the Great Lakes have significantly declined in the past 15 to 20 years. Media in southeastern lower Michigan began reporting that Michigan citizens could now safely eat all the fish they could catch. He suggests that some research project, similar to ones described for consumers, be designed about media.

Dr. Holcomb suggested that the Panel process not be speeded up, but rather that the Panel take all the time it needs to adequately review the available data and do its job right. He also expressed concern about the number of uncertainty factors which have been built into RfD process and that the RfD values are too low for that reason.

Dr. Carlson agreed with Dr. Holcomb. He stated that there were actually several issues of concern, one is the data itself, another is the interpretation of the data and a third is the appropriateness of the uncertainty factors. For some things there will not be clear cut answers for a long time. Dr. Clark responded that even though there are problems with studies in various areas, the data they produce continue to fall within close range of one another. Some people may be trying to reach too fine a point from a public health point of view. Dr. Carlson pointed out that the numbers get close only because small numbers are worked with. It is too hard to communicate to people about orders of magnitude. Dr. Cicmanec commented that the USEPA had once considered using a range instead of one number. It could not be done, because there was no more assurance about the limits of the range.

Dr. Fischer spoke about the potential health benefits to the individual of fish consumption. He cautioned against reducing consumption so low that it caused other harm. He argued for a cost-benefit analysis. He also said he did not believe the Panel's job was easy or could be accomplished as quickly as the Council of Great Lakes Governors wished.

Dr. Clark said the USEPA was not trying to pressure the Panel. The Protocol has been eight years in the making, and just as everyone thought it was finished, it turned out that there was an additional review. The USEPA wants people to be able to eat the fish in the Great Lakes and sees the advisory as shifting consumption to smaller, less contaminated fish.

Mr. Harrison indicated that the charge to the Panel was neither to delay nor speed up implementation of the Protocol by the states, but rather to review and evaluate the adequacy of the science of the Protocol. The states may do whatever they deem advisable in terms of waiting for the outcome of this Panel's review. Scientific knowledge is ever changing and any document which has its basis in science should be periodically reviewed so as to ensure that the science used is the most relevant. The current Protocol has taken eight years to develop. During that time considerable

changes have taken place in our knowledge base and considerable changes have taken place in the Great Lakes environment. These issues need to be considered if the states are to provide the most accurate information to the public about the consumption of Great Lakes fish.

Dr. Carlson brought up the problem of variation in fish consumption due to ethnic background. Dr. Clark said that communicating effectively with various ethnic groups and attaining real behavior change were significant problems, requiring adequate time and resources.

Dr. Knuth inquired about information concerning the shifts in species listed in the Protocol compared with current advisories. Mr. Harrison asked if Mr. John Hesse, Michigan Department of Public Health, could provide such a comparison. Mr. Hesse indicated that he would get the information to the Panel.

Dr. Fischer asked why there had not been any changes made to the Protocol as a result of the two previous reviews. Mr. Hesse responded that the Task Force had thought the reviews would be closer together and had decided to wait for all to be completed before beginning the revisions.

#### **IV      NEXT MEETING DATE**

No date was set for the next meeting of the Panel. Mr. Harrison indicated that his office would poll the Panel members on the best date for everyone.

#### **V        ADJOURNMENT**

The meeting was adjourned at 3:30 p.m.

Keith G. Harrison, M.A., R.S., Cert. Ecol.  
Executive Director  
Michigan Environmental Science Board



**Attachment 1. Presentation by Dr. Henry Anderson, Wisconsin Division of Health and Co-chair of the Great Lakes Fish Advisory Task Force, to the Council of Great Lakes Governors Special Fish Advisory Panel.**

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Dr. Anderson began by explaining that the Protocol is incomplete and not in the form in which it will be ultimately issued. It does not address all compounds of concern, since data bases were inadequate for some of the Great Lakes.

The process used to develop the Protocol has involved the use of the best available data and the judgement of the Task Force members. The old Protocol was severely criticized as having no true scientific basis and not allowing for an estimate or understanding of risk.

The Task Force considered several approaches for the development of the new uniform Protocol. The National Wildlife Federation approach, using a summation of all the potential chemicals and their upper limit of cancer risk, was rejected because it was felt that the results were unrealistically stringent. Both the traditional cancer risk and comparative risk approaches were rejected also. Comparative risk is not easy to analyze meaningfully. The traditional cancer risk analysis has several shortcomings: (1) the public tends not to believe it, (2) it is difficult to get a consensus about acceptable risk levels, and (3) the purpose of an advisory is to elicit behavioral change, so it is not enough to tell people what the risks are and advise them to make their own decisions. Cancer risk became just one of the factors involved in building a health protection value. Another problem was that current advisories often did not have proportional doses and risks among the categories of fish used. The Task Force decided to make the doses proportional, from lowest to highest.

The Task Force wanted to choose one stable reference number to build the advisory on. The Food and Drug Administration (FDA) advised the Task Force not to use its action level in development of the advisory. In addition, the Task Force did not want to use RfDs, since that was the regulatory approach. They decided on the use of a weight of evidence approach and the use of a community of experts to evaluate the data to arrive at what seems to be a good number (referred to as health protection value or HPV) to represent all the data that exist. If the Task Force was to develop the Protocol again, it would choose an established number and let the USEPA defend its scientific validity.

Despite any shortcomings in the Protocol development, the Task Force feels that its developed HPV is very reasonable. It is a number designed to provide protection. The Protocol is driven by PCBs, but that could be changed based on regional circumstances. The HPV incorporates and accommodates all the available human and animal data and is consistent with a cancer risk policy as well. It should be protective for the other chemicals unless they are present in unusually high amounts. It is intended only for the Great Lakes. The Protocol was developed in order to establish a uniform format among the Great Lake states while still allowing for modification due to

local circumstances. It was also designed to be periodically updated as new problems arise or when new data become available.

The Task Force did a survey of Great Lakes states' populations regarding fish consumption in 1993. Based on that survey, Michigan has the largest number of people saying they ate Great Lakes sport fish, but all the states have sizeable fish eating populations. The results indicated that the best way to obtain behavioral change was to teach fish eaters how to clean and prepare the fish to reduce risk. Women are less aware of the advisories than men, since most of the information has been disseminated through fishing licenses, and may not be shared with non-fishers.

## **Attachment 2. Presentation by Dr. Vernon Miller, Michigan State University, to the Council of Great Lakes Governors Special Fish Advisory Panel.**

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Dr. Miller indicated that the purpose of his study was to examine the relationship between awareness of the fish advisory and corresponding behaviors. The study consisted of surveying 401 licensed anglers. The response rate of the survey was 75%. The average age of the respondent was 34, and 80% of the respondents were male and 20% female. Twenty-one percent of the respondents indicated that they fished in one of the Great Lakes.

The key part of the study was to investigate individuals beliefs regarding health risks associated with eating Michigan sport-caught fish. These beliefs were divided into five categories ranging from "no risk at all" to "there is a huge danger". For the phone interviews, risk was divided into three categories: (1) no risk/perfectly safe, (2) conditionally safe (which fish and from where), and (3) some danger, often specifying the risk (mercury, PCB). Based on the results, there appears to be very little concern regarding reproductive risk among those that associated risk to eating Michigan sport-caught fish; there was a general reference to cancer, but none to reproductive issues. When looked at through risk value, the overall perception of risk was 1.94 out of 5.

Respondents were questioned on the source of their information. Newspaper, television, own experience, and fishing regulations were identified as the major sources of information. When compared to the information concerning risk perception from above, those that perceive low risk were those that relied on their own experiences for information, whereas those that perceived higher risks received their information from newspapers or other prime information sources.

In terms of individual fishing behavior, individuals indicated that they fished about seven times over the summer months and typically consumed 2.35 meals on average per month for the entire year. Bluegill, trout, walleye, perch and bass were the preferred fish or target catch.

When questioned specifically about the advisory, there was very little familiarity. Approximately 56% of those polled claimed they had read the fish advisory, which is printed on the back of the license. Of this 56%, the average familiarity with the advisory was 2.7 out of 5, where, "5" would be very familiar and "1" not familiar at all. Of these same respondents, only 29% felt they knew who published the advisory and of this group, 85% said it was produced by the Department of Natural Resources.

In terms of the relationships between behavior and beliefs, it was discovered that even if people had very strong beliefs concerning the danger of Great Lakes fish, this did not translate into significant behavior modification (no impact on the type of fish consumed or frequency of fish consumption). When questioning the subgroup of respondents who had read the advisory, there was no significant altering of behavior, whether a risk was perceived or not.

In summary, individuals tend to have a clear belief system in place concerning the safety or health risk associated with eating Michigan sport-caught fish. However, in terms of their behavior patterns, there is no discernible difference in how much fish they consume in response to this belief system.

### **Attachment 3. Presentation by Dr. John Cicmanec, U.S. Environmental Protection Agency, to the Council of Great Lakes Governors Special Fish Advisory Panel.**

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The reference dose (RfD) for polychlorinated biphenyls (PCBs) was derived from the results of animal research studies by the USEPA Reference Dose/Reference Concentration Work Group. This work group is composed of scientists from all of the Regional offices as well as Program offices such as the Office of Water and Office of Pesticide Programs and Toxic Substances. In addition to deriving reference doses which pertain to potential human oral exposure, the work group also derives reference concentrations for inhalation exposure and methodology is being developed for dermal exposure. As part of the process for establishing an RfD the work Group reviews all of the available research data for a compound such as PCBs as well as the available reports of accidental human exposure. Once an RfD is established by the work group a peer review group will be put together to review the data as well as the risk assessment process.

The specific commercial PCB mixtures for which RfDs have been established by USEPA include Aroclors 1016, 1248, and 1254. An RfD for Aroclor 1260 may be considered in the future. The two primary determinations that have to be made when deriving an RfD are (1) what is the critical adverse effect, and (2) at what dose did the effect occur, hence what lower dose would be a "safe" level of exposure. Ideally data taken from human exposures would be most applicable for human risk assessment, however, such data when available does not provide precise exposure levels and often the exposed individuals were also exposed to other chemicals. The advantage of using animal studies is that doses can be controlled and the test subjects are free from exposure to other substances and free of intercurrent disease. In addition, a wide variety of specimens can be collected from animals during the experiment and the test subjects can be killed at the end of exposure so that a thorough pathologic assessment of tissues can be performed. A reference dose is defined as an estimate, with uncertainty spanning perhaps an order of magnitude, for humans, including sensitive subpopulations, of a daily dose that is likely to be without an adverse health effect throughout a lifetime.

Each PCB mixture is composed of perhaps 20-30 congeners, or different chemical forms depending upon the arrangement of the molecules, out of a possible group of 209 congeners. Depending on the degree of chlorination different PCB mixtures can be put into groups that show the same pattern of toxicity. It is known that the mixtures of PCB congeners that are found in the environment are different than those found in the commercial mixtures. Nevertheless, the toxicity that has been observed in laboratory studies should predict the effects likely to occur for environmental exposures.

Monkey reproductive studies using Aroclor 1248 demonstrated lower birth weights of the infants as well as the neurobehavioral deficits including delayed spatial alternation and discrimination reversal deficiencies. It also appears that prenatal exposure to

Aroclor 1248 may effect sperm production once the infants have reached puberty. In addition to the lower infant birth weights, studies with the lesser chlorinated mixture, Aroclor 1016, have caused specific pathologic lesions in specialized regions of the brain.

When reference doses are developed for various chemicals it is often necessary to apply uncertainty factors to the doses that were tested in the experimental studies in order to establish the correct human dose. Allowance for the use of uncertainty factors include (1) sensitive subpopulations among humans, (2) extrapolation for results of animal studies to humans, (3) adjustment for subchronic exposure to chronic exposure, (4) adjustment from a LOAEL [lowest dose level that caused an effect], if the study design did not include a NOAEL [no observed adverse effect level], and (5) lack of a complete toxicity database.

The RfD for Aroclor 1254 demonstrates some variation in the application of uncertainty factors. The standard factor of 10 is usually applied when results of animal studies are applied to humans. However, rhesus monkeys were used for the Aroclor 1254 studies and because there are several metabolic similarities for rhesus monkeys and humans in uncertainty factor of 3 is more appropriate. In addition, the duration of the critical study was 55 months which is approximately one fourth of the rhesus monkey life span, therefore a reduced uncertainty factor of 3 was used for this adjustment rather than a full factor of ten.

The critical adverse effects that were noted for Aroclor 1254 included ocular discharge accompanied by enlarged ocular sebaceous glands (Meibomian glands) and decreased immune competence as demonstrated by the decreased IgG and IgM antibody levels to injected sheep red blood cells. These changes were noted in the lowest dose group which received 5 micrograms/kg-day of Aroclor 1254. There appears to be a human correlation to the decreased immune competence noted in the rhesus monkeys. A Canadian scientist, Dewailly, has observed a five-fold increased incidence of middle ear infections among Inuit infants that have consumed breast milk contaminated with high levels of PCBs.

**Attachment 4. Overheads used by Dr. John Cicmanec, USEPA, to the Special Fish Advisory Panel (edited).**

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**Aroclor 1016**

**Critical Effects**

- Reduced birth weights
- Neurobehavioral deficits
  - discrimination reversal
  - delayed spatial alternation

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**Aroclor 1016**

**Uncertainty Factors**

- 3x - for sensitive human sub-populations
- 3x - for extrapolation from Rhesus monkeys to humans
- 3x - for extrapolation from sub-chronic to chronic exposure
- 3x - for database deficiencies

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**Aroclor 1254 ( Arnold Study )**

**Immunologic Changes**

- Reduction in and IgG and IgM antibodies to sheep RBCs
- Decrease in percentage of helper T-lymphocytes
- Increase in suppressor T-lymphocytes

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**Aroclor 1254 ( Arnold Study )**

**Clinical Changes**

- Ocular exudate
- Finger and toe nail changes separation from nail bed, prominent nail beds
- Inflamed and prominent Meibomian glands

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**Aroclor 1254**

**Why the antibody response to sheep RBCs is important**

It is an antigen-driven response that requires the interaction of several distinct cell types. These include:

Antigen processing and presentation by macrophages and participation by  
T-helper cells types  
Proliferation and differentiation of B-cells into plasma cells  
Secretion of antibodies specific for sheep RBCs by plasma cells

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## **Aroclor 1254**

### **Uncertainty Factors**

- 10x - for sensitive human sub-populations
- 3x - extrapolation from Rhesus monkeys to humans
- 3x - minimal LOAEL to a NOAEL
- 3x - extrapolation from sub-chronic exposure to chronic exposure